Stengel (A.)

Fever in the Course of Bright's Disease and in Uræmia.

BY

ALFRED STENGEL, M.D.,

INSTRUCTOR IN CLINICAL MEDICINE, UNIVERSITY OF PENNSYLVANIA; ASSISTANT PHYSICIAN TO THE UNIVERSITY HOSPITAL; PHYSICIAN TO THE HOWARD HOSPITAL.

FROM

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES,

NOVEMBER, 1895.

Extracted from The American Journal of the Medical Sciences, November, 1895.

FEVER IN THE COURSE OF BRIGHT'S DISEASE AND IN URÆMIA.

By Alfred Stengel, M.D.,
INSTRUCTOR IN CLINICAL MEDICINE, UNIVERSITY OF PENNSYLVANIA; ASSISTANT PHYSICIAN TO THE UNIVERSITY HOSPITAL; PHYSICIAN TO THE HOWARD HOSPITAL.

Among the many and various symptoms of acute and chronic nephritis that have received special attention the temperature has, comparatively speaking, been neglected, though a few authors have given it considerable study. These will be alluded to more particularly in discussing the various conditions under which fever may occur and the forms it is apt to assume.

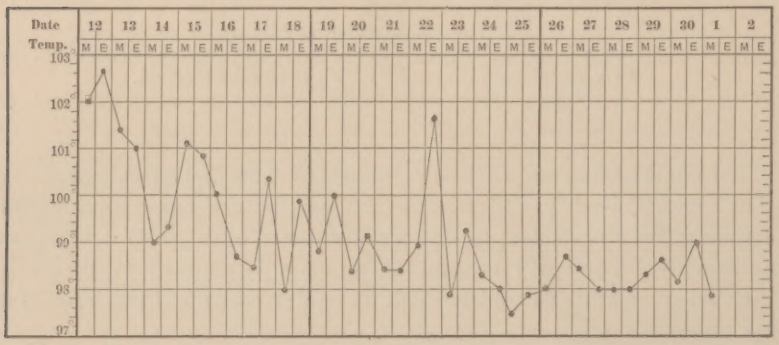
There are three groups of cases of distinct character in which acute or chronic nephritis and elevation of the body temperature are found to be associated. In the first group are included cases of mild febrile reaction at the beginning of acute nephritis; in the second the elevated temperatures result from complicating diseases, while the third and least well recognized group is that in which the temperature is elevated in the course of the uræmic state. It is to the latter that I wish to call attention more particularly in this paper, but it will be interesting, I think, to consider briefly the other groups for the sake of completeness.

I. The temperature at the onset of acute Bright's disease has quite commonly been found to be elevated. This elevation is rarely marked enough to attract more than passing attention, and little study has been made of its causes. Without attempting to enter upon the broad question of the pathogenesis of Bright's disease, we may say that this early slight fever is due either to the inflammatory or degenerative lesion of the kidney, to poisoning of the system, on account of the retention of deleterious substances which the kidney, as a rule, excretes, or, as would sometimes seem probable, from the primary infection or intoxication, which is to be looked upon rather as the cause than as the result of the disease of the kidney. The clinical fact, however, is well known. In the cases appended the type and degree of pyrexia usually observed are well illustrated.

Case I.—W. C., aged thirty-five years, had been out of bed but a few days after recovery from an attack of typhoid fever when he became languid, weak, and, as he expressed his condition, very stupid. In this state he first came under my observation. The urine was greatly reduced in quantity and contained considerable albumin with casts. The man's temperature was at first 102.6° F. It soon declined, however, but remained moderately elevated for over a week, subsiding gradually.

During this time there was also a gradual increase in the quantity of the urine, and the patient's general condition steadily improved. He recovered entirely in a short time.

CHART I.



CASE II.—M. D., aged thirty-five years, had noticed for several months increasing difficulty in putting on his shoes, but he really had not thought himself ill until three weeks before his entrance into the hospital. At that time there was decided swelling of the feet, which later involved the legs and scrotum, and was soon followed by vomiting, pain inthe back, and headache. The urine was scanty, acid in reaction, and contained considerable albumin. The specific gravity was 1020. The patient was extremely pale, and had decidedly the appearance of a nephritic. The arteries were a little stiffened and the ventricle hypertrophied. After a few weeks the dropsy and other symptoms had improved so much that the patient was discharged from the hospital. In this case it seemed evident that the man had a chronic form of nephritis, and that the present attack was of the nature of an acute congestive or inflammatory exacerbation. There were none of the ordinary indications of a uræmic state. The temperature in this case, also, was above the normal for several days, but fell as the urine increased in quantity and the dropsy disappeared.

CASE III.—M. C., a young woman, having a subacute form of nephritis was exposed to the weather and became thoroughly chilled. Shortly afterward there was considerable pain in the back, and the urine showed increase of albumin, with blood cells. The temperature at the same time rose to 102° F., and varied between this and the normal for two days.

Such degrees of fever at the onset of acute nephritis are usual and well known. In some instances, however, the primary fever is very marked, and may be quite alarming. This is especially the case in the primary bacterial nephritis of Bamberger, Aufrecht, Litten, Babes, Perret, and Mannaberg, or infectious nephritis, as Friessinger calls it. In these cases, indeed, there is little doubt but that these are instances of infectious diseases localizing themselves in the kidneys from the first. Sometimes, as in the series reported by Friessinger, there is distinct

epidemicity, and various micro-organisms have been isolated in such cases. It is in these infectious cases that high fever may occur at the onset. Friessinger[1] records one in which it reached 105° F., and in which the symptoms of infection were very marked.

II. A second variety of fever in the course of nephritis is that which owes its origin to inflammatory complications, such as pericarditis, pleuritis, pneumonia, or the like. There may also be temporary elevations of the temperature, resulting from some renal complication, such as acute exacerbations in chronic nephritis, the development of pyelitis, or the deposit of chalky material in the course of a gouty Bright's disease. Sometimes these inflammatory complications may be so latent that their existence remains unrecognized, and the cause of the elevated temperature is undiscovered until autopsy is performed. Some authors have invoked this tendency to latency of inflammatory complications to explain the high fever of some of the forms of uræmia presently to be described; but it is to be noted that the fever resulting from inflammatory complications in Bright's disease are apt to be very low, especially in comparison with that seen in similar conditions in the course of rheumatism, whereas the cases to which this theory has been applied are just the ones in which hyperpyrexia is most commonly observed. I do not dwell longer on this question, as it is, after all, aside from the present discussion, and for the same reason it is unnecessary to instance cases.

III. The third condition under which fever is likely to occur in the course of Bright's disease, and it is to this I have wished most particularly to call attention, is the state ordinarily known as uræmia. Before entering upon this question in its clinical aspects it may be of interest to review hastily the various theories that have been offered in explanation of this condition. One of the oldest and best known is that of Traube. This would explain the manifestations of uræmia on a mechanical basis, ascribing them to a state of repletion of the vessels and œdema of the brain, inducing a secondary condition of anæmia of the brain substance. This theory was based on the discovery in some cases of conditions such as described, particularly in autopsies on persons dead of uræmic convulsions; and it seemed to receive a measure of support from the investigations of Munck, and Otto and Bidder, who found that injection of water into the cervical vessels induced symptoms not unlike those of uræmia. The theory, however, is disproved by the fact that many cases do not present the œdematous conditions of the membranes or brain-substance described, and more particularly by the observation of Carter,[2] of Liverpool, that analysis of the cerebral substance does not show a disproportionate amount of serosity after uræmic convulsions. The experimental evidence cited loses its force when we recognize that the quantities of water injected are alone capable of inducing toxic mani-

festations. After Traube various chemical theories have been brought forward. One thought that ammonia was the noxious agent, another ascribed the symptoms to potassium poisoning, another to creatin, creatinin, urea, and so on. That none of these theories is satisfactory to explain the manifestations of uræmia is apparent enough when we study the experiments of the many who have worked in this field. It is true that each of these substances may act as a toxic agent when injected in sufficient quantity, but none is capable of reproducing the exact manifestations of uræmia. Bouchard,[3] who has done so much in this field, thinks that there are at least seven toxic substances in the normal urine. These are: 1, a diuretic substance (urea); 2, a narcotic poison; 3, a sialogogue; 4, a temperature-reducing substance; 5 and 6, convulsants (one, doubtless, potassium), and 7, a poison which causes contraction of the pupil. However this may be, and no doubt all of these substances do exist in the urine, none of them can be looked upon as the cause of uræmia. Recently Hughes and Carter[4] have added very important facts to the elucidation of the nature of uræmia. According to them the active poison is probably an albuminous substance quite different from any which exists in the normal urine.

In all of these investigations it has been assumed that the temperature in uræmia is reduced, and no doubt this is usually the case. A few investigators have, however, studied the question of urine-intoxication with special reference to the temperature. Binet[5] showed that human urine contains a substance which may be precipitated, dissolved in glycerin and reprecipitated with alcohol, and which has the power of causing elevation of the temperature in guinea-pigs. It is most abundant in the urine of tuberculous individuals, and is most active in tuberculous guinea-pigs. The temperature usually begins to rise after two hours, reaches its height in about three hours, and subsides after four or five. He regards it as of the nature of a ferment, and calls attention to the fact that various ferments (pepsin and trypsin, Bergmann and Angerer, fibrin ferment, Edelberg, bacterial ferments, Charrin, Ruffer, Hildebrand, Roussy and others) have been found to have similar pyretogenous properties, and that some of these occur in the urine at times. Lepine[6] sought to escape some of the objections that may be urged against other methods by injecting sterile normal salt solution into the ureters of a dog under pressure sufficient to insure a steady entrance of the liquid. Injection of the same amount of sterile salt solution directly into the veins of a dog did not cause the symptoms (dyspnœa and fever), and he concludes that there are pyretogenous substances in the urine. He was further able to induce fever by injection of extract of the kidneys of a normal dog. This experiment is open to several objections. Bouchard, and latterly Hughes and Carter, injected the urine itself into the veins, and found very constantly fall of the temperature. Binet would explain this by

the assumption that there are both fever-provoking and temperature-reducing substances in the urine, and that the latter usually dominate.

Clinically, the occurrence of fever in the course of uræmia has been known to exist for a long time, but little attention was paid to it. Lees called attention to it in 1852, but authors generally rarely referred to the temperature until the publication of the well-known papers of Bourneville,[7] in 1872. This author claimed that depression of the body-heat is a constant phenomenon of uræmia, and, indeed, made this the basis for denying the uræmic nature of eclampsia. Later writers, all or most, at least, agree that many cases of uræmia are attended with elevation of temperature. This change of view is chiefly attributable to the writings of Bartels,[8] who maintained that he had seen but one case of uræmic convulsions in which the temperature was not elevated. There is, however, much difference of opinion as to the cause of the fever, many holding that it is usually due to complications. This view, while it is true of some cases, is not true of most, for numerous instances are recorded where careful search was made after death for some local lesion to explain the fever. I think that the majority of authorities would now admit without question the existence of fever of purely uræmic origin, and the tendency of the day is to assign as the cause of this some toxic excitation of the heat-regulating apparatus, rather than cerebral or meningeal congestion, or the like. One very striking evidence of the toxic, rather than organic, character of the fever in uræmia is the precise manner in which the temperature frequently follows the increase or decrease of the uræmic state and the very rapidity of the rise and decline. That congestion of the meninges or œdema of the brain is not the immediate cause of the fever is evident from the facts that, while in cases reported by Chantemesse and Tenneson,[9] and by Richardiere and Therese,[10] there was one or the other of these conditions; in those of Bouveret[11] and of Dumont[12] no lesion was discovered, and Carter, in his chemical analysis, failed to find excess of water in the brain substance.

Bartels called attention to the clinical fact that very frequently uræmic symptoms develop rapidly when there is rapid subsidence of the dropsy, and ascribes this to the liberation of poisonous substances contained in the cellular œdema. In such cases there is apt to be some elevation of temperature, which Bartels would ascribe to the intoxication; but Carter thinks this due rather to the hot vapor baths, and cites a case in point. That this view is not an accurate one is apparent in the following case under my observation. In this there was decided rise of temperature coincidently with the rapid decline of dropsy, and for which there was no adequate explanation excepting that indicated. No hot-air bath had been used, and the temperature became normal as soon as the œdema was completely discharged.

Case IV.—P. M., aged twenty-six years, a driver, had led a very exposed life; had had a chancre two years previous to his coming under my observation; but was not excessive in the use of alcohol, and had really had no serious illness except pneumonia a few years before. Six months before he had pain in the back and other vague symptoms, which disturbed him for a time, but subsided spontaneously. The illness which brought him under my notice began on the night of November 6th, after he had been exposed to the weather. He thought he had taken "cold," and had considerable cough. The next day his face was swollen, and later the legs and abdomen. The urine was very scanty, high colored, the specific gravity was 1034, there was much albumin and hyaline, granular and epithelial casts. The anasarca became marked; there was occasionally great dyspnœa. No lesion of the heart or lungs was discovered on physical examination. The treatment instituted was purgation and sweating with pilocarpin. After a day or two of normal temperature there was a slight rise, which soon subsided, and then the temperature was normal for ten days. At the end of that time there was a sudden rise to 101° F., coincident with the establishment for the first time of free diaphoresis by the aid of pilocarpin. The amount of liquid discharged through the skin was truly remarkable, as was also the rapidity with which the anasarca disappeared. During the four or five days in which the dropsy was subsiding the temperature remained elevated, and after the complete disappearance of œdema the temperature became normal, and convalescence was soon complete. The patient was discharged entirely well, and was still so a year later.

Whatever solution may eventually be found for the existence of fever in certain cases of uræmia, I am for the present more concerned with establishing the clinical fact that there are certain cases of uræmia in which the temperature is elevated in the absence of any complication and irrespective of the inflammatory condition of the kidney itself. It is a well-recognized clinical fact, first clearly established by Bourneville, that the temperature in uræmia is usually depressed below the normal, but it should be recognized that the reverse may be the case, and that in the course of chronic Bright's disease a sudden elevation of the temperature without any discoverable cause may be due to uræmia. It is impossible at the present time to say why there is elevation of the temperature in some and depression in others; nor is it possible to indicate any features in which the febrile cases differ from the afebrile excepting the temperature, for exactly the same clinical manifestations that are seen in the febrile cases are often present without any elevation of the temperature. It is possible, however, to distinguish two classes of cases as far as the temperature is concerned; those in which the onset is very sudden and the symptoms pronounced, and those in which the approach is insidious or the symptoms of a depressive character.

I. The first or eclamptic form is most frequently present in cases of uræmia with convulsions, as Bartels pointed out, but there may be just as decided fever in comatose or delirious cases in which no convulsion occurs. Many cases of this form of uræmic fever are recorded, but I

select the following, in which the temperature was specially observed, to indicate the character of the attacks.

Richardiere and Therese report a case of acute nephritis following exposure to cold, in which the temperature from the first was entirely normal, and remained so until the patient developed signs of urœmia. The temperature then rose to 102.2° F., after which convulsions developed and there was a further rise of the temperature to 104° F. After five days there was a critical decline of fever, and the temperature again remained normal until a second attack of uræmia was announced by dimness of vision, headache, and a rise of temperature to 101.2° F. This attack was aborted by prompt venesection. In their second case there were the signs of interstitial nephritis, with œdema of the legs and scrotum. For some time the temperature was normal, then the patient became delirious; he refused to stay in bed, and shortly afterward or coincidentally the temperature suddenly rose to 103.6° F. There was also epistaxis. The day following epileptiform convulsions were noted, and the uræmic state continued for five days, finally yielding to venesection.

Mousson [13] reports a case in which there were dropsy, pleural effusion, considerable albuminuria with blood cells. After five days of normal temperature there was a sudden elevation to 103.6° F. with coma, epistaxis, and convulsions. Subsequently there was Cheyne-Stokes breathing, and the patient was bled. The temperature fell quickly and remained but little above the normal for a day or two, when it subsided completely. In this case the first elevation of the temperature occurred before the first convulsion.

Gillet [14] reports a case in a man of twenty-eight years, in which there was stupor followed by convulsions. The temperature was between 99° and 100° F. There was bloody expectoration and some soft râles at the bases of the lungs; the urine was highly albuminous. The temperature rose during the two days following until it reached 105.8° F., when the patient died. The autopsy disclosed interstitial nephritis, œdema of the bases of the lungs, and some meningeal congestion.

In these cases of typical eclamptic fever it will be noted that the temperature in reality began to rise before the onset of the convulsions, which cannot, therefore, be regarded as causing the elevation of temperature by the violence of the muscular movements. In the first case of Richardiere and Therese this was further disproved by the subsequent abortive attack in which the temperature rose without convulsions, subsiding promptly after venesection. Similar cases have been recorded by Dumont, Carter, Amidon, Wiener, Hughes, and others. The two following from my own experience are instructive and to the point.

Case V.—T. D., aged thirty-seven years, was brought to the hospital by the ambulance at 11 A.M. June 6th. He was decidedly stuperous;

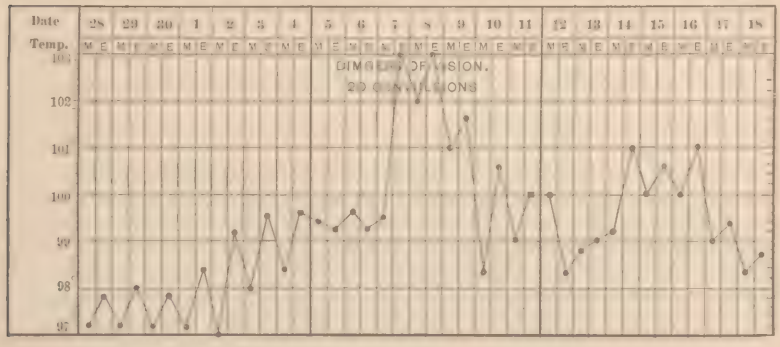
the breathing was heavy, somewhat stertorous; the skin was moist, the pupils of ordinary size and responsive. The patient was catheterized, and the urine found to be scanty, heavy, and albuminous. The man was evidently in an uræmic condition, and was therefore placed in a vapor bath, and perspired very freely; but despite this favorable action he rapidly sank into a condition of complete unconsciousness and became convulsed. Convulsions followed in rapid succession during two hours after his admission, in spite of the administration of nitrite of amyl, chloroform, and chloral; and the patient was finally bled after the eighth convulsion, nine fluidounces of blood being removed. At once there was decided improvement. An abortive convulsion, which was readily controlled by inhalation of chloroform, occurred five minutes after the venesection, but the patient almost immediately afterward became conscious, and remained so during most of the day. The next night there was another series of convulsions, beginning about ten o'clock. After the fourth the patient was again bled (nine fluidounces), after which there were but two light fits. On the night of the 10th, three days later, there were three slight convulsions, after which the patient recovered. Repeated examinations of the urine confirmed the diagnosis first made of chronic parenchymatous nephritis; and though most careful physical examination was made no complication of any kind was discovered in the other organs. The point of particular interest in this case for the present was the behavior of the temperature. On admission this was found to be 100.1° F., but almost immediately it began to rise. The elevation really began before the first convulsion, but the greatest elevation was not reached until some time after the beginning of the fits, when it was 106.6° F. After the cessation of the convulsions there was a rapid decline of the temperature to about 100° F. The next day there was another rise of the temperature without fits to 102° F., and during the night when the second series of convulsions occurred the temperature rose to 102.6° F. After this the temperature was subnormal until the last series of fits, when it rose again, but only to the normal.

Case VI.—J. O., aged twenty-six years, a laboring man, giving a good family history; had himself led a very irregular life. He had worked in various parts of coal-mines from an early age; was habitually much exposed, and drank excessively of ale. In December of 1892 he became thoroughly wet and chilled and took "cold." This was not unusual, as he had had chronic cough, beginning at a time when he worked in the dust of the "breakers." About January 1, 1893, he put himself under the care of a medical man, but did not improve, and on the contrary noticed that his weight was increasing and that his face was growing puffed. Soon his feet became swollen, and subsequently the whole body, his weight increasing twenty pounds.

When he first came under my care, in February, his appearance was that of a man having the anasarca of renal disease; his color was very white, the blood examination showing 3,350,000 erythrocytes, 10,000 leukocytes, and 53 per cent. of hæmoglobin; there was a puffed condition of the face and neck and universal œdema. The urine was below the normal in quantity, varying from twenty to forty ounces; it was loaded with albumin and contained hyaline, granular, and blood casts. The patient was troubled with considerable cough, and on examination of his chest there were dry and moist bronchial râles, with evidences of slight emphysema. The heart was healthy, but the second sound

markedly accented, and the pulse so tense that it was difficult to determine the existence or absence of hardening of the vessel wall. He was ordered diuretic and purgative treatment, but the condition remained practically unchanged during several months. His temperature during

CHART II.



this time was almost constantly below the normal, and never above that point. On the first day of May the temperature rose to the normal, and the next day was 99.2 F. At the same time the patient complained of pain in one of his teeth, and then of headache. These symptoms continued for five days, the temperature remaining at about 99° F. On the 7th, in the morning, there was sudden dimness of vision, followed by an uræmic convulsion, and after this by a number of others during the day and the following night—twenty in all. He was put in a hot vapor bath, was bled about twenty fluidounces, was given croton oil, and purged with salines, and received chloral by the rectum. The next day he was wholly conscious and continued to improve. The temperature, which had been about 99° F. before the first convulsion, rose shortly after the onset of the latter to 103° F., where it remained the next day. For several days after this it was elevated, though not so much. Subsequently there was a rise of temperature due to mastoiditis, but excepting this there were no further unpleasant symptoms, the temperature remained normal or below the normal, and the patient finally recovered almost entirely.

In each of these, again, it is noted that the rise of temperature began before the first convulsion and the second one is particularly instructive and significant in that there was a period of five days of slight fever with mild uraemic symptoms before the convulsions began. Indeed, my previous experiences with febrile temperature before violent uræmia led me to predict its occurrence in this case three days before the first convulsion.

In the following cases there was similar, sudden fever, running an acute course, but without any convulsions. In these, of course, the old theory of convulsive fever cannot be entertained at all.

Bouveret reports the case of a woman who came to the hospital with well defined indications of chronic interstitial nephritis. There was considerable gastric irritability, vomiting, etc., and the temperature was 102.8° F. The following day the symptoms increased and the temperature continued elevated. This continued four days, when the temperature rose to 108.6° F., and the patient became comatose and died. At the time of death the thermometer registered 109.6° F., while an hour later it was 110° F. There was at no time any tendency to convulsion. At the autopsy there was found a high grade of contraction of the kidneys and some œdema of the lungs, together with hypertrophy of the heart, but no lesion of any other organ or structure including the brain cord and their membranes.

Richardiere and Therese record one case in their series having the clinical features of chronic interstitial nephritis, in which uræmia was suddenly developed in the form of coma, Cheyne-Stokes respirations, and sudden elevation of the temperature to 102.2° F. There were no convulsions, and the temperature remained between 102° and 103° F. for three days, when the patient died. Autopsy revealed the lesions of chronic interstitial nephritis, and there was some sub-arachnoid effusion of serum.

Chantemesse and Tenneson detail an interesting case occurring in a young woman of thirty-one years, who had had slight and transient œdema without albuminuria shortly before the delivery of twins. Eleven days after the labor there was pain in the brachial plexus and back of the neck, with large albuminuria and somewhat fetid lochia. During the next five days there were shifting palsies, mostly hemiplegic, loss of consciousness, dimness of vision, and ascending fever. The temperature finally reached 105.2° F. on the sixth day, and the patient perished. At the autopsy the kidneys were swollen and congested, and there was congestion of the membranes and substance of the brain and cord.

In a second case a man of sixty-six years who had had two previous attacks of unconsciousness became suddenly comatose, and showed diminution of sensation with loss of power on the right side. There was decided albuminuria. The temperature was 104.8° F. in the rectum, and later 106.2° F. At the autopsy arterio-sclerotic kidneys, atheroma of the aorta, some congestion of the bases of the lungs, and dropsy of the ventricles were detected.

In a third case the temperature rose during an attack of coma and hemilateral convulsions to 100.2° F., and remained between this point and 99° F. for over two weeks, during which the patient was more or less stuperous, but not convulsed. There was decided albuminuria. The patient passed from their observation shortly afterward.

A striking case of sudden uræmia, with delirium and high fever, terminating after free diaphoresis was observed by Damaschino.[15]

I have seen several cases of sudden uræmic coma with similar eclamptic fever, but have not preserved accurate clinical notes of any.

It will be seen from a study of the cases detailed that the temperature in this variety of uræmic fever rises more gradually than would at first seem to be the case. In nearly all, whether there are convulsions or not, there is an elevation for one or several days of a degree or two. When convulsions set in they are, as a rule, preceded by sharp rise of

temperature to 102°, 103° or 104° F., and following the fit there is generally still more elevation, sometimes to 105°, 106° or 107° F. In fatal cases the high temperatures persist to the end, and there may be a further rise of a degree or more after death. In cases that are not fatal the temperature declines very soon and reaches the normal in a day or two unless the convulsions or other signs of the intoxication persist, when the temperature may also continue elevated.

II. The second form of febrile uræmia alluded to is that in which the onset is rather insidious, or at least not attended with the violent symptoms seen in the eclamptic cases, and in which the clinical manifestations are rather those of a slow infectious process not unlike those seen in the typhoid state. Systematic writers speak of such cases in reference to the differential diagnosis of typhoid fever (Osler[16], Pepper[17], Chantemesse[18]); but the literature does not furnish many accurately studied cases. In these cases the patient is frequently delirious, the tongue is dry and coated, the bowels constipated or relaxed, and the resemblance to an asthenic febrile disease like typhoid fever may be very close. The symptoms and the features by which the differential diagnosis is made will be better described in connection with the cases to be detailed.

A case of this kind, but without fever, was observed by Richardiere[19] in a young child of eleven years. The prominent symptoms in this were dropsy, stupor, delirium and headache, but there was no elevation of the temperature. Another case in which delirium occupied a prominent part in the clinical history of the case was recorded by Derignac[20], but this also was afebrile. Recently Josipovici[21] records a case of uræmia with the clinical features of an infectious disease, and Roch[22] published a contribution, to which I could not gain access, on the typhoid form of uræmia. The following cases of my own, however, suffice to indicate the nature of this form of uræmia.

Case VII.—T. P., aged seventy-three years, was admitted to my care, complaining of great heaviness and torpor. There was nothing of interest in his family history. He had had Chagres fever in South America many years before. Five years before the present illness he had an attack of unconsciousness, which lasted several hours. Since that time he had had frequent attacks of shortness of breath, sometimes very extreme, and cough, with frothy expectoration. There was also considerable epigastric soreness.

On admission the man was in a stupid condition, and there was considerable dyspnœa. The tongue was dry and covered with a brown fur; the bowels were a little loose; the pulse was slow and tense. Little urine could be obtained, but it was decidedly albuminous. On physical examination a rather high grade of pulmonary emphysema was determined, and there were besides soft, moist râles throughout both lungs. The heart-action was irregular, and the size of the organ difficult to determine on account of the emphysema of the lungs. The skin of the patient was dry and harsh; the temperature normal.

In the afternoon the patient began to wander in his mind, and there was slight fever. During the night there was very decided delirium, and the man could be kept in bed only with great difficulty. These symptoms persisted for two weeks, after which the patient died. The only new symptom was vomiting, which was noted one day. The prominent features of the case were the continuous delirium, the great depression, the restlessness, the dry-coated tongue, all of which gave the case a decided resemblance to typhoid fever on casual examination. There was, however, no enlargement of the spleen; there was no eruption of any kind, and the diarrhœa was not of the usual character met with in this disease. The pupils were small; the urine was constantly decreased in amount. Death occurred after two weeks of practically the same symptoms, apparently from exhaustion.

Autopsy. Emaciated old man; chest of the barrel-shape character. On opening the thorax the heart was seen to distend the pericardial sac, and on removal was found greatly hypertrophied, the wall of the left ventricle being two inches thick. There was no valvular disease of any kind. The heart weighed twenty-two ounces; the lungs were slightly œdematous; the kidneys were small, rather light in color, and the left contained a small retention cyst. On section the cortical substance was found to be of a light color and seemingly very fatty; the vessels in the kidney substance were patulous and stiff. The capsule was somewhat adherent. Weight of the kidneys: left, three and one-half ounces; right, six ounces.

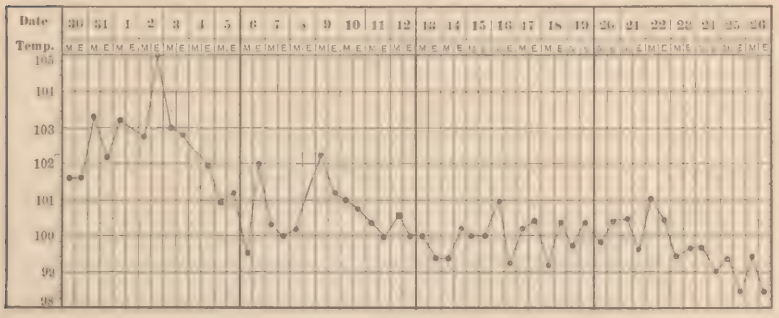
The temperature in this case was never high, though on several occasions it passed 99° F.; but the other symptoms were so decidedly typhoidal that I venture to include it in the group of slow febrile uræmia.

A second case is more striking and deserves to be reported in detail:

Case VIII.—Mrs. S. was admitted to the gynecological wards as a supposed case of sepsis on July 30, 1894. She passed through a normal labor two months previously, and seemed to have recovered when the present condition of fever and depression was developed. On admission to the hospital the temperature was 101.6° F., the respirations 34, and the pulse 100; the patient was in a stuperous or almost comatose condition, there was occasional twitching of the hands and feet, especially on one side, and the body was covered with an eruption of sudemia and miliaria. The tongue was coated but moist. Physical examination revealed a rather harsh form of inspiratory murmur, but no other indication of pulmonary disturbance. The pulse was quite tense, and the second aortic sound was accentuated, but there was no murmur. The pupils were about normal in size and somewhat sluggish in action; the abdomen was flat—there was no pain or tenderness; the spleen was not enlarged; the bowels had been costive for several days. There was a urinous odor about the patient which was not decided, but still suggestive. The urine was scanty and had a specific gravity of 1018; it contained abundant albumin and hyaline and granular casts in very large numbers. The provisional diagnosis of uræmia was made, and the patient was ordered Rochelle salts in hourly doses of a drachm each, with the result that she had twenty large, watery stools in the next twenty-four hours. Very soon the stuperous condition cleared away, the pulse softened, the respirations grew more regular and natural in sound, and the twitching ceased entirely.

Further examination of the patient was now made. The blood was found to contain 4,300,000 red corpuscles and 17,400 leucocytes. The stained blood showed about the same proportion of lymphocytes, large and small, polynuclear elements and eosinophilous forms in a count of several hundred leucocytes.

CHART III.



On vaginal examination a contracted, hard, and slightly retroverted uterus was discovered, and there was no vaginal discharge. Abdominal examination still continued negative. The urine still presented the same large albuminuria and abundance of casts. The temperature was kept under control by sponging, which was repeated twenty-three times in the first three days. After this time no more sponging was needed. With the improvement in the patient's general condition there was a subsidence in the rapidity of the pulse and a fall in the temperature. After the fourth day the former fell to between 60 and 80 in the minute. The respirations continued rapid, but were far more natural in character. There was no more twitching. On August 10th there appeared a painful swelling of the calf of the left leg. This extended upward along the line of the femoral vein, which could be felt as a hardened cord. There was some slight coldness and blueness of the foot, but under treatment by rest, elevation, and sedative applications, all symptoms subsided after a few days.

The patient's general condition improved immediately after the first thorough purgation, and still more after the administration of digitalis, beginning August 3d. The albumin gradually decreased in amount, and was sometimes absent entirely. When the patient was finally discharged there were neither casts nor albumin. The urine was examined for pepton with negative result. The blood at the second examination showed 3,300,000 red corpuscles and 31,200 leucocytes, with 70 per cent. of hæmoglobin.

Clinically this case suggested three possibilities: typhoid fever, puerperal sepsis, and uræmia. The diagnosis seemed to me to rest with the last condition. The appearance of the patient at once, however, suggested typhoid fever, and so strikingly that it was more difficult to eliminate this than the clinical report would indicate. The absence, however, of splenic enlargement, of intestinal symptoms, of rose spots,

and the presence of distinct leucocytosis were points of considerable importance in the diagnosis. Of course the possibility of primary typhoid fever with secondary nephritis and consequent uræmia made the evidences of uræmia, that were unmistakably present, of no value in the exclusion of typhoid fever. The frequency of phlebitis and thrombosis in typhoid fever and their infrequency in nephritis would, of course, have some value in the diagnosis. I find, however, in the records of Prof. Tyson, at the University Hospital, a case of pure nephritis in which femoral thrombosis and gangrene developed while he was under observation in the hospital. The points indicated, however, served to set this disease aside, and the subsequent history of the case was confirmatory. The question of puerperal sepsis was perhaps even more troublesome. There was not, it is true, any evidence of gross infection with uterine or parauterine disease, since the gynecologist reported the uterus and its appendages normal; but the possibility of infection without marked local reaction, and with particular or sole involvement of the kidneys, as in some of the reported cases of infectious nephritis, required careful consideration. It was to be remembered in the first place that the diagnosis was concerned with the state of the patient at the time of her entrance into the hospital rather than with the determination of the original cause of her disease. There was undoubtedly a condition of acute nephritis, possibly of infectious origin; but the question to be decided was whether the associated symptoms were due to uræmia or to infection, no matter whether the primary nephritis were infectious or not. My opinion of this matter was very promptly formed. The woman was undoubtedly uræmic, as the condition of the mind, the twitching, the odor of the patient's skin and breath, and the scanty albuminous urine indicated. The effect of treatment served only to strengthen this opinion, for almost at once, after the first thorough purgation, the stupor, twitching, and odor disappeared, as might be expected in uræmic conditions, but scarcely in pure sepsis. I say nothing of the subsidence of the temperature, though I regard this also as significant, for the reason that it is my present purpose to establish the significance of fever in uræmia, rather than to form deductions from its presence or absence. After the first decline of the fever and subsidence of the uræmic symptoms it will be noted that there was a continuance of a milder degree of fever. This may have been due to lingering uræmic intoxication or to the continued existence of infection or of an inflammatory condition of the kidneys. It seems to me not in the least unlikely that the last assumption may have considerable foundation, but it is impossible to settle the question definitely. The earlier typhoidal symptoms, however, seem undoubtedly to have been uræmic, since they disappeared so promptly and with such exact correspondence to the degree of purgation; the substratum of infectious nephritis, with the fever proper to it, would not be influenced

in the same prompt and decided manner, and, would therefore, remain after the removal of the uræmic element. The idea of sepsis entering even into the causation of the nephritis itself seems to me to be negatived by the fact that the labor was normal and had preceded the first indication of kidney trouble by fully two months; and still more by the fact that the patient presented none of the usual indications of sepsis.

SUMMARY.—Fever may occur in the course of Bright's disease under three conditions: 1. At the onset of acute nephritis as a result of the infection or intoxication causing the disease, or of the inflammatory or degenerative lesions in the kidney themselves; 2, in the course of acute or chronic Bright's disease as a result of various complications; and, 3, in uræmia. The fever associated with uræmia may be sudden and pronounced, and associated with coma, delirium, or convulsions — eclamptic fever; or it may be more general, more lasting, less marked, and associated with typhoidal symptoms—slow uræmic fever.

LITERATURE.

1. *Friessinger:* Gaz. Méd. de Paris, 1889, p. 313.
2. *Carter:* Brit. Med. Journ., 1888, ii. 463–469.
3. *Bouchard:* Auto-intoxication in Disease. Translated by Oliver.
4. *Hughes and Carter:* Amer. Journ. Med. Soc., August, 1894.
5. *Binet:* Rev. méd. de la Suisse romand., October, 1892.
6. *Lepine:* Rev. de Méd., 1889, p. 514.
7. *Bourneville:* Étude Clin. et Thérmomet. sur les Mal. du Syst. Nerv. Duexieme Partie. Uræmie, etc., 1872.
8. *Bartels:* Ziemssen's Cyclopœdia.
9. *Chantemesse and Tenneson:* Rev. de Méd., 1885, p. 935.
10. *Richardière and Thérsèe:* Rev. de Méd., 1891, p. 991.
11. *Bouveret:* Lyon Méd., 1889, p. 75.
12. *Dumont:* Journ. de Méd. de Bordeaux, 1882.
13. *Mousson:* France Méd., 1885, p. 509.
14. *Gillet:* Rev. de Méd., 1892, p. 163.
15. *Damaschino:* Cited by Mousson.
16. *Osler:* Text-book on Medicine.
17. *Pepper:* American Text-book of Medicine.
18. *Chantemesse:* Traité de Méd.
19. *Richardière:* L'Union Méd., lxi. 253.
20. *Derignac:* Limousin Méd., 1891, xv. 163.
21. *Josipovici:* Inaug. Dissert. Berlin, 1894.
22. *Roche:* Bull. de la Soc. méd. de l'Yonne, 1887.